

J. WALLACE PAGE  
USSN To be Assigned  
Page 4

R2  
one  
84. The method of claim 83 further comprising the step of detecting said first product particles using single particle detection.

85. The method of claim 78 further comprising the step of analyzing said residual primary stream.

#### REMARKS

With this amendment, claims 75-85 are pending in the application. New claims 75-85 are copied from claims 1-4 and 7-13 of U.S. Patent No. 6,221,677, with the following modifications. First, the claims and dependencies are renumbered to conform to claim numbering in the present case and to the claims which are presented.

Second, the wording of certain claims is modified as noted in detail in Table 1.

Support for the new claims can be found throughout the specification. Table 1 below, sets forth claims from the '677 patent and the present claims along with example support for each claim limitation as found in the present specification. In addition to the support referenced in Table 1, additional support for many, if not all of the limitations, can be found in other portions of the claims and specification as filed. Therefore, no new matter is added to the specification by the new claims and Applicants respectfully request that the claims be entered.

Please note that in Table 1, bracketed language appears in the indicated claim of the '677 patent, but is omitted from the corresponding claim in the present application.

Underlined language is present in the new claims presented herewith, but not in the corresponding claim in the '677 patent.

Respectfully submitted,



Gulshan H. Shaver  
Reg. No. 37,496

CALIPER TECHNOLOGIES CORP.  
605 Fairchild Drive  
Mountain View, CA 94043  
Ph: (650) 623-0675  
Fax: (650) 623-0500  
GHS:mc

U.S. Patent No.6,221,677	Present Application
<p>Claim 1 of '677 patent. Claim 75 in present application.</p> <p>conducting said primary stream into a laminar flow reaction channel;</p> <p>separately conducting a reagent stream comprising reagent particles into said reaction channel, such that said primary stream and said reagent stream flow in adjacent laminar streams;</p> <p>allowing said primary particles to diffuse from said primary stream into said reagent stream, and to react with said reagent particles and form detectable product particles, thereby converting said reagent stream into a product stream and said primary stream into a residual primary stream;</p> <p>conducting said residual primary stream out of said reaction channel;</p> <p>separately conducting said product stream out of said reaction channel; and</p> <p>detecting said product particles.</p>	<p>The present invention provides methods for performing various biochemical analyses. One example is a receptor/ligand binding assay comprising antibody/antigen pairs. See page 7, line 29 through page 8, line 3 and page 10, lines 14-16.</p> <p>Figure 2B, elements 106, 114 and accompanying text on page 24, lines 32-34 describe conducting a primary stream into a laminar flow reaction channel. Support for microscale channel dimensions is provided on page 14, lines 27-35 wherein channels having cross sectional dimensions in the range of <math>0.1\mu\text{m}</math> to about <math>500\mu\text{m}</math> are described.</p> <p>Figure 2A, elements 104 and accompanying text on page 24, lines 29-30 illustrates conducting a reagent stream comprising receptor particles into the reagent channel 110 wherein the reagent stream flows in adjacent laminar stream with the primary stream. Also, see Figure 5 and text on page 26, lines 11-15.</p> <p>See Figure 5 and accompanying text on page 26, lines 25-29.</p> <p>Figure 5 illustrates conducting a residual primary stream out of reaction channel 510b and into channel region lying between the intersection of channel 510 with channel 526 and reservoir 518.</p> <p>The product stream for example, sample plugs containing the receptor and the ligand are flowed out of reaction channel 510b and into the transfer channel 526. See Figure 5 and text on page 26, lines 29-38.</p> <p>See page 24, lines 34-37 and Figure 2A.</p>

Claim 2 of '677 patent. Claim 76 in present application.	The method of claim 1/75 further comprising the step of analyzing said residual primary stream.	Page 27, lines 21-24 describes post reaction analysis. Also see description of the system on page 36, lines 27-31.
Claim 3 of '677 patent. Claim 77 in present application.	The method of claim 1/75 wherein said primary stream <u>comprises components of a biochemical system [is blood]</u> , said small primary particles are native antigens, and said first reagent particles are first antibodies.	See page 10, lines 14-16 for examples of receptor/ligand interactions assayed using methods of the present invention including antibody/antigen binding pairs. See also, page 7, lines 10-24 for description of biochemical systems.
Claim 4 of '677 patent. Claim 78 in present application.	<p>A method for reacting primary particles from a primary stream, comprising the steps of:</p> <p>conducting said primary stream into a first laminar flow reaction channel;</p> <p>separately conducting a first reagent stream comprising first reagent particles into said first laminar flow reaction channel, such that said primary stream and said first reagent stream flow in adjacent laminar streams;</p> <p>allowing said primary particles to diffuse from said primary stream into said first reagent stream, and to react with said first reagent particles and form first product particles, thereby converting said first reagent stream into a first product stream and said primary stream into a residual primary stream;</p> <p>thereafter conducting a first companion stream into said first laminar flow reaction channel such that said first product stream and said first companion stream flow in adjacent laminar streams thereby converting said first product stream into a diffused first product stream and said first</p>	<p>The present invention provides methods for performing various biochemical analyses. One example is a receptor/ligand binding assay. See page 7, line 29 through page 8, line 3 and page 10, lines 14-16.</p> <p>Figure 2B, elements 106, 114 and accompanying text on page 24, lines 32-34 describe conducting a primary stream into a laminar flow reaction channel. Support for microscale channel dimensions is provided on page 14, lines 27-35 wherein channels having cross sectional dimensions in the range of 0.1µm to about 500µm are described.</p> <p>Figure 2A, elements 104 and accompanying text on page 24, lines 29-30 illustrates conducting a reagent stream comprising receptor particles into the reagent channel 110 wherein the reagent stream flows in adjacent laminar stream with the primary stream. Also, see Figure 5 and text on page 26, lines 11-15.</p> <p>See Figure 5 and accompanying text on page 25, line 9 for description of formation of a first product stream comprising receptor/labeled ligand. Also see page 26, lines 25-29.</p> <p>See page 24, lines 27-37 describing companion stream comprising test compounds being conducted into the laminar flow reaction channel such that the first product stream of receptor/ligand flow in adjacent laminar streams with the companion stream</p>

	<p>companion stream into a diffused first companion stream;</p> <p>conducting said residual primary stream out of said first reaction channel; and</p> <p>separately conducting said first diffused product stream out of said first reaction channel.</p>	<p>thereby converting the first product stream into a diffused product stream and the companion stream into a diffused companion stream.</p> <p>Figure 5 illustrates conducting a residual primary stream out of reaction channel 510b and into channel region lying between the intersection of channel 510 with channel 526 and reservoir 518.</p> <p>The product stream for example, sample plugs containing the receptor and the ligand are flowed out of reaction channel 510b and into the transfer channel 526. See Figure 5 and text on page 26, lines 29-38.</p>
Claim 7 of '677 patent. Claim 79 in present application.	The method of claim 4/78 wherein said primary stream contains larger, non-diffusing particles in addition to said primary particles.	See page 29, lines 26-31 for a description of primary streams containing larger particles such as beads. Also see page 7, lines 10-24 for description of biochemical systems that are used in the methods of the present invention.
Claim 8 of '677 patent. Claim 80 in present application.	The method of claim 7/79 wherein said primary stream <u>[is blood]</u> comprises components of a biochemical system, said primary particles are native antigens, and said first reagent particles are first antibodies.	See page 10, lines 14-16 for description of antibody/antigen binding pairs. Also see page 24, lines 27-28. See also, page 7, lines 10-24 for description of biochemical systems.
Claim 9 of '677 patent. Claim 81 in present application.	The method of claim 4/78 wherein said step of detecting said first product particles comprises a method selected from the group consisting of optical, electrical, calorimetric and <u>chemical detection</u> .	See page 17, lines 9-28 for description of various detection systems comprising optical and calorimetric detection.
Claim 10 of '677 patent. Claim 82 in present application.	The method of claim 4/78 wherein said step of detecting comprises absorbance, <u>luminescence</u> or fluorescence detection.	See page 17, lines 9-28 for description of various detection methods comprising absorbance and fluorescence.
Claim 11 of '677 patent. Claim 83 in present application.	The method of claim 4/78 wherein said first reagent particles are immobilized on beads.	See page 29, lines 26-31 for a description of bead based biochemical systems.
Claim 12 of '677 patent. Claim 84 in present application.	The method of claim 11/83 further comprising the step of detecting said first product particles using single particle detection.	See page 32, lines 25 –37 for description of particles using single particle detection such as individual identification of spent beads.

Claim 13 of '677 patent. Claim 85 in present application.	The method of claim 4/78 further comprising the step of analyzing said residual primary stream.	Page 27, lines 21-24 describes post reaction analysis. Also see description of the system on page 36, lines 27-31.
--	---	--